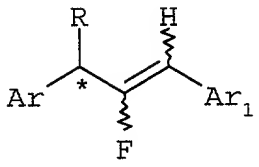
WHAT IS CLAIMED IS:

1. A process for the preparation of a chiral compound of formula I



I

wherein

Ar is phenyl optionally substituted with any combination of from one to three halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy, C_1-C_4haloalkoxy or hydroxy groups,

1- or 2-naphthyl optionally substituted with any combination of from one to three halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups, or

a 5- or 6-membered heteroaromatic ring optionally substituted with any combination of from one to three halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups;

R is C_1-C_4alkyl, C_1-C_4haloalkyl, C_3-C_6cycloalkyl or C_3-C_6halocycloalkyl;

Ar_1 is phenoxyphenyl optionally substituted with any combination of from one to six halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups,

phenyl optionally substituted with any combination of from one to five halogen, C_1-C_4alkyl,

C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups,

biphenyl optionally substituted with any combination of from one to five halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups,

phenoxypyridyl optionally substituted with any combination of from one to five halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups,

benzylpyridyl optionally substituted with any combination of from one to five halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups,

benzylphenyl optionally substituted with any combination of from one to five halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups,

benzoylphenyl optionally substituted with any combination of from one to five halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups,

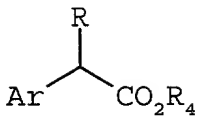
1- or 2-naphthyl optionally substituted with any combination of from one to three halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups, or

a 5- or 6-membered heteroaromatic ring optionally substituted with any combination of from one to three halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups, and

the (E)- and (Z)- isomers thereof,

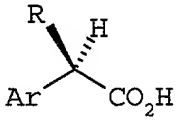
which process comprises the following steps:

a) treating a racemic ester of formula II



II

wherein Ar and R are defined as hereinabove and R_4 is C_1-C_4alkyl with an esterase to form a first mixture of either R-acid IIIa and S-ester IIIb



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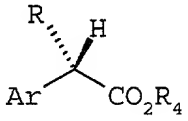
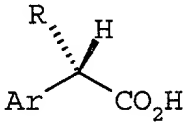
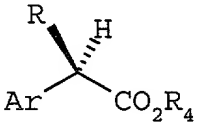


IIIa IIIb

or of S-acid IIIc and R-ester IIId



and

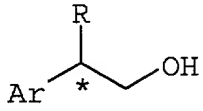


;

IIIc IIId

b) separating said acid IIIa or IIIc from said ester IIIb or IIId;

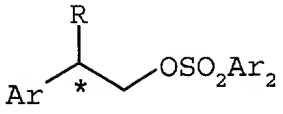
c) reducing said acid IIIa or IIIc or said ester IIIb or IIId to obtain a chiral alcohol IV having the R- or S-configuration



IV

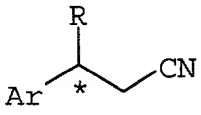
d) reacting said chiral alcohol with an arylsulfonyl halide Ar_2SO_2X

wherein Ar_2 is phenyl, p-chlorophenyl, or p-tolyl, and X is chloro, bromo or fluoro to afford a sulfonate of formula V



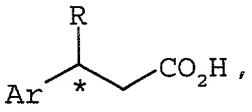
V

e) reacting said sulfonate V with a cyanide-delivering agent to afford a nitrile of formula VI



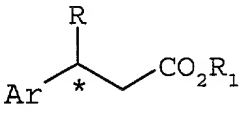
VI

f) hydrolyzing said nitrile VI to afford an acid of formula VII



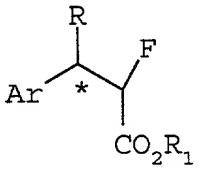
VII

g) esterifying said acid VII with an alcohol R_1OH, wherein R_1 is C_1-C_4 alkyl to afford an ester of formula VIII



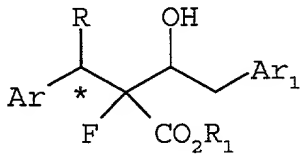
VIII

h) fluorinating said ester to afford a fluoro-ester of formula IX



IX

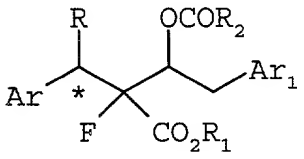
i) reacting said fluoro ester with an aldehyde Ar_1CH_2CHO, wherein Ar_1 is defined as hereinabove, in a solvent in the presence of a base to afford a second mixture of 4 chiral diastereomeric hydroxy-esters of formula X;



X,

j) optionally separating said second mixture X into a third mixture Xa and a forth mixture Xb, each mixture having two chiral diastereomers;

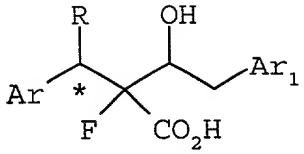
k) treating said hydroxy-ester mixture X, Xa or Xb with an acylating agent R_2COX_1, wherein R_2 is C_1-C_4alkyl and X_1 is Cl, Br or R_2COO, to afford a fifth mixture of 4 chiral diastereomeric acyloxy esters XI, a sixth mixture of 2 acyloxy esters of formula XIa, or a seventh mixture of 2 chiral diastereomeric acyloxy esters XIb



XI,

l) optionally separating said sixth or seventh mixture into essentially pure chiral diastereomeric acyloxy esters;

m) hydrolyzing said pure chiral acyloxy esters or mixtures of esters of formula XI to afford a hydroxy-acid of formula XII,



XII

and

n) heating said hydroxy-acid XII with an arylsulfonyl halide $Ar_3SO_2X_2$, wherein Ar_3 is phenyl, p-chlorophenyl, or p-tolyl, and X_2 is chloro or bromo to afford the desired chiral compound of formula I.

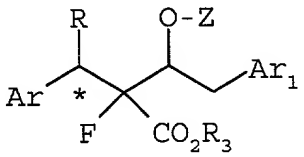
2. The process according to claim 1 wherein said esterase is horse liver esterase.

3. The process according to claim 1 wherein said base is lithium diisopropylamide.

4. The process according to claim 1 wherein said solvent is tetrahydrofuran.

5. The process according to claim 1 wherein R_4 is methyl.

6. A chiral compound of the following formula



XIII

wherein

Ar is phenyl optionally substituted with any combination of from one to three halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy, C_1-C_4haloalkoxy or hydroxy groups,

1- or 2-naphthyl optionally substituted with any combination of from one to three halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups, or

a 5- or 6-membered heteroaromatic ring optionally substituted with any combination of from one to three halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups;

R is C_1-C_4alkyl, C_1-C_4haloalkyl, C_3-C_6cycloalkyl or C_3-C_6halocycloalkyl;

Ar_1 is phenoxyphenyl optionally substituted with any combination of from one to six halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups,

phenyl optionally substituted with any combination of from one to five halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups,

biphenyl optionally substituted with any combination of from one to five halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups,

phenoxypyridyl optionally substituted with any combination of from one to five halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups,

benzylpyridyl optionally substituted with any combination of from one to five halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups,

benzylphenyl optionally substituted with any combination of from one to five halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups,

benzoylphenyl optionally substituted with any combination of from one to five halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups,

1- or 2-naphthyl optionally substituted with any combination of from one to three halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups, or

a 5- or 6-membered heteroaromatic ring optionally substituted with any combination of from one to three halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups, and

R_3 is H or C_1-C_4 alkyl; and

Z is H or COR_2, wherein R_2 is C_1-C_4 alkyl.

7. The compound according to claim 6 wherein Ar is phenyl optionally substituted with any combination of from one to three halogen, C_1-C_4alkyl, C_1-C_4haloalkyl, C_1-C_4alkoxy or C_1-C_4haloalkoxy groups; and

R is C_1-C_4alkyl or C_3-C_6cycloalkyl.

8. The compound according to claim 7 wherein Ar_1 is phenyl optionally substituted with one to three halogen groups; and

R is C_3-C_6cycloalkyl.

9. The compound according to claim 8 selected from the group consisting of

methyl (2S,3S)-2[(R)-(4-chlorophenyl)(cyclopropyl)-methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-butanoate;

methyl (2R,3R)-2-[(R)-(4-chlorophenyl)(cyclopropyl)-methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-butanoate;

methyl (2S,3R)-2-[(R)-(4-chlorophenyl)(cyclopropyl)-methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-butanoate;

methyl (2R,3S)-2-[(R)-(4-chlorophenyl)(cyclopropyl)-methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-butanoate;

methyl (2S,3S)-2-[(S)-(4-chlorophenyl)(cyclopropyl)-methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-butanoate;

methyl (2R,3R)-2-[(S)-(4-chlorophenyl)(cyclopropyl)-methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-butanoate;

methyl (2S,3R)-2-[(S)-(4-chlorophenyl)(cyclopropyl)-methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-butanoate;

methyl (2R,3S)-2-[(S)-(4-chlorophenyl)(cyclopropyl)-methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-butanoate;

methyl(2S,3S)-3-(acetyloxy)-2-[(S)-(4-chlorophenyl)-(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)butanoate;

methyl(2R,3R)-3-(acetyloxy)-2-[(S)-(4-chlorophenyl)-(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)butanoate;

methyl(2R,3R)-3-(acetyloxy)-2-[(S)-(4-chlorophenyl)-(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)butanoate;

methyl(2S,3R)-3-(acetyloxy)-2-[(S)-(4-chlorophenyl)-(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)butanoate;

methyl(2S,3S)-3-(acetyloxy)-2-[(R)-(4-chlorophenyl)-(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)butanoate;

methyl(2R,3R)-3-(acetyloxy)-2-[(R)-(4-chlorophenyl)-(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)butanoate;

methyl(2R,3S)-3-(acetyloxy)-2-[(R)-(4-chlorophenyl)-(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)butanoate;

methyl(2S,3R)-3-(acetyloxy)-2-[(R)-(4-chlorophenyl)-(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)butanoate;

(2S,3S)-2-[(S)-(4-chlorophenyl)(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-3-hydroxy-butanoic acid;

(2R,3R)-2-[(S)-(4-chlorophenyl)(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-3-hydroxy-butanoic acid;

(2R,3S)-2-[(S)-(4-chlorophenyl)(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-3-hydroxy-butanoic acid;

(2S,3R)-2-[(S)-(4-chlorophenyl)(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-3-hydroxy-butanoic acid;

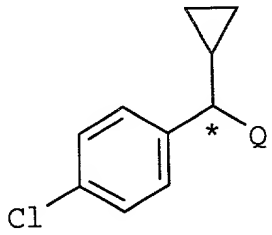
(2S,3S)-2-[(R)-(4-chlorophenyl)(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-3-hydroxy-butanoic acid;

(2R,3R)-2-[(R)-(4-chlorophenyl)(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-3-hydroxy-butanoic acid;

(2R,3S)-2-[(R)-(4-chlorophenyl)(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-3-hydroxy-butanoic acid; and

(2S,3R)-2-[(R)-(4-chlorophenyl)(cyclopropyl)methyl]-2-fluoro-4-(4-fluoro-3-phenoxyphenyl)-3-hydroxy-butanoic acid.

10. A chiral compound of the following formula



wherein

Q is $-CO_2H$; $-CO_2CH_3$; $-CH_2OH$; $-CH_2OSO_2Ar_2$; $-CH_2CN$; $-CH_2CO_2H$; $-CH_2CO_2R_1$; or $-CHFCO_2R_1$;

Ar_2 is phenyl, p-chlorophenyl or p-tolyl; and

R_1 is C_1-C_4alkyl.

11. The compound according to claim 10 selected from the group consisting of

(2R)-2-(4-chlorophenyl)-2-cyclopropylethyl 4-methylbenzenesulfonate;

(2S)-2-(4-chlorophenyl)-2-cyclopropylethyl 4-methylbenzenesulfonate;

(3R)-3-(4-chlorophenyl)-3-cyclopropylpropanenitrile;

(3S)-3-(4-chlorophenyl)-3-cyclopropylpropanenitrile;

(3R)-3-(4-chlorophenyl)-3-cyclopropylpropanoic acid;

(3S)-3-(4-chlorophenyl)-3-cyclopropylpropanoic acid;

methyl (3R)-3-(4-chlorophenyl)-3-cyclopropylpropanoate;

methyl (3S)-3-(4-chlorophenyl)-3-cyclopropylpropanoate;

methyl (3R)-3-(4-chlorophenyl)-3-cyclopropyl-2-fluoropropanoate; and
methyl(3S)-3-(4-chlorophenyl)-3-cyclopropyl-2-fluoropropanoate.